

Carlos Chagas and the discovery of Chagas's disease (American trypanosomiasis)¹

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In 1979 we celebrated not only the 100th anniversary of the birth of Carlos Chagas (Figure 1), but also the 70th anniversary of his discovery of the flagellate, *Trypanosoma cruzi*, and the memorable events that followed.

Carlos Justiniano Ribeiro Chagas was born on 9 July 1879, in the small town of Oliveira, Minas Gerais, in Brazil. His father owned a small coffee plantation, and died when Carlos was not yet 4 years old, leaving his mother widowed at 24 with four small children, of whom Carlos was the eldest. His childhood and youth were uneventful: though not rich, the family was by no means poor; after her husband's death, Carlos's mother carried on with the coffee



Figure 1. Carlos Chagas in 1932.
(Reproduced from Chagas Filho 1959)

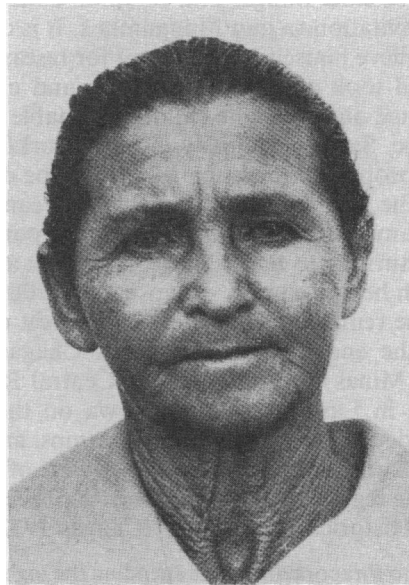


Figure 2. Berenice, aged 53 (1960).
(Reproduced from Salgado *et al.* 1962)

plantation. It was his mother's wish that Carlos study mining engineering, but early on, at the entreaties of a physician-uncle who pointed out to him that for Brazil to develop it was necessary to rid the country of the endemic diseases which were blocking all progress, he switched to medicine.

In 1896, when Chagas entered the Faculty of Medicine in Rio de Janeiro, Brazil was a country of ten million inhabitants, and Rio a small poor town whose port, like all Brazilian ports, was a hotbed of infectious disease. Yellow fever was rife; smallpox and bubonic plague, among other scourges, were epidemic if not endemic; immigrant as well as native populations

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were periodically decimated, making any major social or economic enterprise impossible. No wonder European ships refused to dock in Brazilian ports.

The Faculty of Medicine in Rio was then undergoing a profound transformation, with the introduction of practical (bedside) teaching and pathological anatomy. The teachers, mostly young, were also men of politics and letters, poets, philosophers, as well as physicians; their stimulating influence left its permanent mark on Chagas's cultural formation. In 1902, his academic studies behind him, he chose the haematological aspects of malaria as the subject for his MD thesis. Chagas's contributions to malariology, overshadowed by his discovery of American trypanosomiasis, were by no means trivial, including as they did descriptions of the oedematous form of Quartan fever, the bone-marrow lesions of malaria, and the description of the disease as a domiciliary infection, rarely contracted outdoors. In 1902, he first met Oswaldo Cruz, who was just starting on the gigantic task of ridding Brazilian ports of yellow fever by the systematic combat of the mosquito vector and isolation of the victims in special hospitals, and of smallpox and plague by the introduction of mass vaccination. The eradication of yellow fever was a spectacular success, though the fight against the mosquito was carried on for many years.

In 1902, Oswaldo Cruz, only 7 years Chagas's senior, was working at Manguinhos, the institute mainly devoted to the production of sera and vaccines, which was later to bear his name: Instituto Oswaldo Cruz. After taking over the institute, Oswaldo Cruz was to realize a cherished dream: the development of Manguinhos into a centre of experimental and preventive medicine. Chagas and Oswaldo Cruz became friends at once, but Chagas refused Cruz's first invitation to join Manguinhos. It is characteristic of the modesty of the man that he did not believe himself to be cut out for research; moreover, he felt more drawn to clinical medicine, and took a small hospital job and opened a private surgery. In 1905, however, already married and with one child, and unable to make ends meet, he accepted the offer of the Docas de Santos company, whose workforce was being decimated by malaria, to undertake a prophylactic campaign against the disease in the labourers's camps. At 26, Chagas carried out the first successful anti-malaria campaign in Brazil, which enabled the Santos Docks company to complete the work on the port which was even then the most important in Brazil. On returning to Rio, Chagas was given a similar task in the work on the Xerem river dam, in which he was equally successful. In 1906 he finally joined the Oswaldo Cruz Institute, with which he remained associated for the rest of his life.

Towards the end of 1907, Cruz put Chagas in charge of a prophylactic anti-malaria campaign in Minas Gerais, where the Central Railway was extending its lines. He made his headquarters in Lassance, a small town on the banks of the São Francisco river, where malaria was devastating the labourers' camps, and where he was to repeat his feats of Santos and Xerem. It was there he first became aware of the 'barbeiro', a blood-sucking bug infesting the huts of the region, called the 'barber bug' because of its predilection for biting the victim's face. In his 'Historical Retrospect' (Chagas 1922) he wrote:

'On a journey to Pirapora and while spending the night in an engineers' camp Dr. Belisario Penna and I first made the acquaintance of the *barbeiro*, shown to us by Dr. Cantarino Motta, chief of the engineering committee. Once we heard of the blood-sucking habits of this insect and of its proliferation in human dwelling-places, we became very interested in knowing its exact biology and above all in ascertaining if by any chance it were, as I immediately supposed, a transmitter of any parasite of man or of another vertebrate.'

What followed is well known, but it may be worth recalling some essential facts. In the hindgut of the 'barber' bug, Chagas found a new species of trypanosome, which he named *cruzi* in honour of his friend and mentor, Oswaldo Cruz. It remained to show whether it was pathogenic to vertebrates and, in particular, to man: Chagas found the trypanosome in the blood of a cat and, soon afterwards, in that of a girl of two whom he had seen a fortnight earlier, in the hut where he found the infected cat. This was Berenice. In a perfect rehearsal of Koch's postulates, he succeeded in reproducing the infection experimentally in small animals and in recovering and identifying the parasite from these animals. 1909 saw his preliminary

publications and the first of his great reports (Chagas 1909*a, b, c*) on the disease in man, with a description of the acute form, as well as the morphology and cyclical development of the trypanosome in the intermediate and definitive hosts, attempts at culture of the flagellate, the course of the infection in laboratory animals, and so forth. Two years later (Chagas 1911) he published the definitive description of the clinical, aetiological, pathological and epidemiological features of the disease. The same number of the *Memórias do Instituto Oswaldo Cruz* carried Gaspar Vianna's (1911) minute description of the pathology of Chagas's disease, illustrated by Castro Silva's Plates (e.g. Figures 3 and 4). Brief mention must be made here of the presentation of papers in the *Memórias* at that time, a treasure trove of precision, elegance and style both as regards language (papers were printed side-by-side in Portuguese and German, translated by Adolpho Lutz, himself a distinguished scientist) and the sheer beauty of Castro Silva's plates, the man who 'drew only what he saw'.

I shall not dwell on Chagas's success, which was enormous, both in Brazil and abroad (for some of the details *see* Lewinsohn 1979.) Nor shall I go into the attacks on Chagas by a German microbiologist and his colleagues (Kraus *et al.* 1915, Kraus & Rosenbusch 1917, Kraus 1926), which were later taken up by a clique of Brazilian doctors in the National Academy of Medicine, inspired by ignorance and jealousy of his scientific success and his enormous popularity. I should, however, like to point to some of the features of Chagas's discovery, which make it unique in the annals of the history of medicine. It is usual for a doctor or doctors to start with a number of more or less well-known signs and symptoms ('the effect') whose aetiology ('the cause'), clinical features, natural history, pathology and, in the case of infectious disease, intermediate host(s), reservoir, vector(s) and mode of transmission are the subject of research by many individuals or teams. In the short space of two years, Chagas, almost single-handed, accomplished all this. What is even more remarkable,

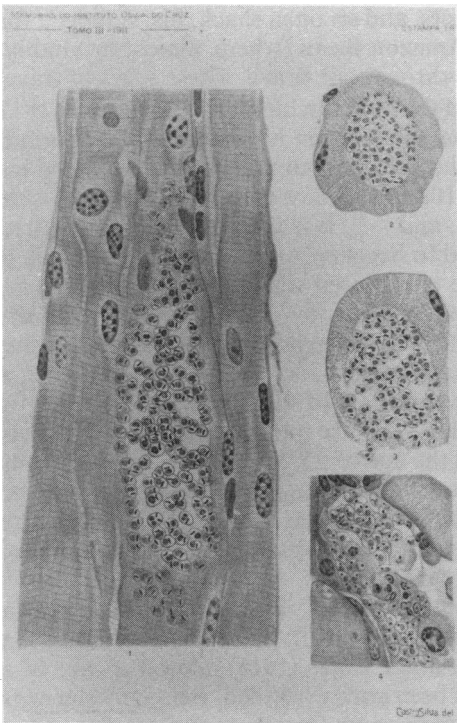


Figure 3. Longitudinal and transverse sections of guinea-pig striated muscle, heavily parasitized by trypanosomes. (Reproduced from Vianna 1911)



Figure 4. Oblique section of guinea-pig seminiferous tubule (1). Section of guinea-pig tunica albuginea (2). Spermatozoa from guinea-pig epididymal tubule (3). (Reproduced from Vianna 1911)

however, is that he started, so to speak, at the wrong end: with a (possible) vector of a (possible) pathogen, causing a disease yet to be discovered and described.

No less remarkable than the discovery of Chagas's disease is, perhaps, the fact that Berenice, in whom he first diagnosed the human disease, is still alive today, more than 70 years later. In 1961 (Figure 2), then aged 53, she was found to be living in Minas Gerais, and was persuaded by a group of doctors in Belo Horizonte to submit to exhaustive tests (Salgado *et al.* 1962) which brought to light the astonishing fact – confirmed in more recent examinations – that the state of carrier of Chagas's disease for fifty, and now over seventy, years is compatible not only with survival but with what can only be described as 'well-being'. Even more surprising is the fact that, whereas her clinical examination was normal, and no cardiac, digestive or other manifestations of acute or chronic Chagas's disease could be found, Berenice's complement fixation (Machado-Guerreiro) test was positive, and trypanosomes obtained from her blood by xenodiagnosis have been cultured, thus starting the 'Berenice' strain. The complement fixation test on her husband, Berenice's first cousin, was negative, but her only son's was positive. She lives with her son and three grandchildren, all of whom are in good health.

It cannot of course be denied that Chagas's intimate knowledge of malaria must have contributed to his intuitive grasp of the situation; and his speculations, as described in his 'Historical Retrospect' (Chagas 1922), on the 'barber' bug as a transmitter of disease were unquestionably inspired by his knowledge of the transmission of malaria and the developmental cycles of the plasmodium in mosquito and man. Nevertheless, his feat remains unique, the fruit of a self-imposed ascetic discipline which was the harsher owing to the unbelievable poverty of means with which he had to contend. Dedication is not uncommon among researchers, but his was extraordinary. For years he lived away from his family, although passionately devoted to them: the four years surrounding the discovery were spent in a railway waggon, his 'laboratory' and living quarters, and an open shack, his 'surgery'; for two years he lived on barges and river boats in the Amazon Basin (where, almost inevitably, he contracted malaria); and he spent years travelling throughout Brazil. These years of travel and life in the hinterland of Brazil, before he assumed the directorship of the Institute in 1917 on Oswaldo Cruz's death, definitely moulded his character. From his diaries of that period, two short passages (Chagas Filho 1959) give an insight into the compassion that pervaded his work and life: 'Side by side with matchless bounty, [there are] dire deficiencies; side by side with exuberant life, death is constantly on the prey'; and '... it is there, in regions invested with Nature's incomparable gifts, that man is reduced to beggary, the race is destroyed, life is extinguished and immeasurable riches lie idle in the unexplored soil ...'

However, far from sinking into sentimental despondency over the immensity of the problems with which tropical medicine is faced, he was a tireless fighter for preventive medicine. His compassion was equalled by his revolt at statistics such as that of São Felipe, a tiny community of 850 to 900 souls, which in the first half of 1911 lost over 400 of its inhabitants to infectious – in Chagas's words, avoidable – disease (probably malaria) (Chagas Filho 1959). A few years before his death in 1934, at the age of 55, he saw one of his dreams come true: the Faculty of Medicine in Rio created a Chair in Tropical Medicine, which he held until his death. His interests ranged widely throughout tropical medicine; his last efforts went towards the establishment of an International Centre of Leprology in Rio de Janeiro, which he directed until his death.

His claim to immortality, however, rests firmly on his discovery of American trypanosomiasis. Despite the attacks on Chagas's work (see above), there was little doubt, in Brazil or abroad, of the importance of his discovery; and Chagas (1911) himself speaks of a 'new realm' in human pathology, a concept which has been amply justified, especially since his death. But neither he, nor Oswaldo Cruz, nor the Brazilian or foreign scientists of the time (the great Koch himself, when told by Hartmann of Chagas's discovery, called a meeting of his assistants at his house the same evening for Hartmann to describe and discuss the new disease), could have foreseen the importance of American trypanosomiasis in years to come. In 1960 a WHO report estimated that 35 million people were at risk, of whom at least seven

million were thought to be infected. As to its prevalence and incidence, the following paragraph from the 1969 WHO report states the situation clearly:

'The prevalence of Chagas's disease, particularly in South America, is far greater than was formerly supposed, and it has been estimated that up to seven million people may harbour *Trypanosoma (S.) cruzi* infections. Although the mortality resulting from the acute form of the disease may be less than 10%, the long-term social and economic effects of the chronic stages are incalculable. Furthermore, the distribution of the arthropod vectors and the occurrence of *T. (S.) cruzi* in animals are more widespread throughout the Americas than is the extent of human infection, presenting a further epidemiological threat.

The most tragic consideration is that, 70 years after its discovery, no drug is available to treat – let alone cure – the disease. On the other hand, like so many 'tropical' diseases, it is no longer a purely medical question, but essentially an economical and political problem. The 'barber' bug has become domesticated, but only lives in human dwellings with cracks and crevices in their walls; plastering and whitewashing the walls, and providing ceilings instead of grass roofs, would go a long way towards diminishing if not eradicating a disease which spells endless misery and sudden death to hundreds of thousands of human beings, and exposure to which is a very real threat to millions.

However, I cannot end on a note of despair. Our hope lies in carrying on the fight, and there to inspire us are the lives of Chagas and others like him, shining examples of what it is possible for the human spirit to achieve in the face of adversity. The fact that it was possible for an obscure doctor, trained only in an underdeveloped country at a time of great instability, living and working in the backwoods without any significant material means, to produce work of such outstanding quality, remains one of the glories of medicine.

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